Compatible ABO Mismatch and Liver Transplantation: a Single Center's Experience

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Objectives: **The current shortage of suitable donor organs and clinical urgency can lead to implanting grafts from ABO-mismatched donors. One-year graft survival rates for patients in this scenario have been reported as ranging between 25% and 75% less than those for ABO-identical or ABO-compatible grafts. We review and compare our experiences with transplanting ABO-identical and ABO-compatible mismatched livers.**

Materials and Methods: **Considering orthotopic liver transplantation (OLTx), 520 were performed at our institution between November 1992 and May 2003, 55 of which were ABO-compatible mismatched transplants. We retrospectively reviewed the data and compared patient and graft survival rates.**

Results: **Overall 1-month and 1-, 5-, and 10-year patient survival rates among identical (group 1) and mismatched (group 2) groups were 97% and 91%, 90%, and 88.5%, and 79%, and 74%, 66%, and 65%, respectively. No significant difference existed between the 2 groups ($P > .05$). Similarly, 1-month, and 1-, 5-, and 10-year graft survival rates among groups 1 and 2 were 96% and 87%, 89% and 83%, 78% and 71% and 66% and 59%, respectively; these were not significant either ($P > .05$). All of the patients in the mismatched group had a high status according to the United Network for Organ Sharing (UNOS). Only 1 person received an incompatible mismatched graft (B to A), which subsequently developed primary nonfunction.**

Conclusions: **ABO-compatible mismatch OLTx is unavoidable given the current state of organ shortage. Our results suggest that this type of OLTx can be performed with minimal risk among patients who require urgent transplantation and have high rankings according to the UNOS and the model for end-stage liver disease (MELD) system.**

Key words: *Orthotopic liver transplantation, ABO-compatible mismatch, Incompatible mismatch*

Ideally, organ grafting should be performed between a recipient and a donor of identical blood groups to minimize the influence of blood-group–specific antigens on graft and patient survival rates. The shortage of suitable donor organs and clinical urgency can lead to implantation of grafts from ABO-mismatched donors [1, 2]. In liver transplantation, it has been suggested that patient and graft survival is diminished with the implantation of ABO-incompatible grafts. Indeed, 1-year graft survival rates in this scenario have been reported to range between 25% and 75% less than those of ABO-identical or ABO-compatible grafts [3]. Here, we review and compare our experience with transplantation of ABO-identical and ABO-compatible mismatched livers.

Materials and Methods

The records of the 520 orthotopic liver transplantations (OLTx) performed between November 1992 and May 2003 at Integris Baptist Medical Center, Nazih Zuhdi Transplantation Institute in Oklahoma City, Oklahoma, were retrospectively reviewed. Group 1 consisted of 465 patients receiving OLTx using ABO-identical grafts, and group 2 consisted of 55 patients receiving OLTx utilizing ABO-mismatched grafts. Within the second group, there were 54 ABO-compat-

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ible mismatched and only 1 ABO-incompatible mismatched liver transplantations. Patients' demographics; diagnoses; complications; causes of death; and 1-month and 1-, 3-, and 5-year patient and graft survival rates were recorded for each group. Total plasma exchange was performed in all patients needing a bridge to liver retransplantation. This was accomplished with the technical support of the Oklahoma Blood Institute, using a COBE Spectra® Apheresis System (Gambro BCT, Lakewood, Colo, USA). The anticoagulant used was 3% citrate phosphate double dextrose in the replacement fluid of fresh frozen plasma.

Statistical Analyses

The Kaplan-Meier Survival test was used to determine patient and graft survival rates. The Wilcoxon rank sum test was used to determine significance between the groups. Values for *P* lower than .05 were accepted as significant.

Results

In group 1, 445 patients (215 males and 230 females; mean age, 44.7 ± 16.4 years; range, 1 month to 71 years) underwent a total of 465 OLTx. In this group, 44 patients (10%) were younger than 18 years of age, and 401 patients (90%) were older than 18 years. Of the 465 grafts, 445 (96%) were primary grafts, 19 (4%) were second grafts, and only 1 patient (0.2%) required a third graft.

In group 2, 50 patients (26 males, 24 females; mean age, 43.3 ± 19.4 years; range, 3 months to 67 years) underwent a total of 55 OLTx. In this group, 5 patients were younger than 18 years of age, and 45 were older than 18 years. Of these 55 grafts, 44 (80%) were primary grafts (including 1 from an O+ donor to an A2 recipient), 10 (18%) were second grafts (of which 9 were ABO-compatible mismatched, and 1 was an ABO-incompatible mismatched [B+ donor to A- recipient]), and only 1 patient (0.2%) required a third graft (which was also an ABO-compatible mismatch).

The etiologies of underlying liver disease for patients in group 2 are summarized in Table 1. Fulminant hepatic failure and autoimmune liver disease were the most common diseases in this group. Of note is the fact that there were no major complications observed during total plasma exchange.

Overall 1-month and 1-, 5-, and 10-year patient survival rates among patients in groups 1 and 2 were 97% and 91%, 90% and 88%, 80% and 74%, and 66% and 65%, respectively. There were no statistically significant differences between the 2 groups ($P > .05$) (Figure 1). Similarly, 1-month and 1-, 5-, and 10-year graft survival rates among patients in groups 1 and 2 were 96% and 87%, 89% and 83%, 78% and 71%, and 66% and 59%, respectively. Although the graft survival rates were lower in patients in group 2 than they were in patients in group 1, the differences were not significant ($P > .05$) (Figure 2).

As mentioned earlier, only 1 patient received an ABO-incompatible mismatched OLTx in this series. He was a 55-year-old white man who had required emergency retransplantation owing to primary nonfunction of the original graft. After the transplantation of this second graft, he developed hyperacute rejection and required a third OLTx. All patients in the mismatched group had a high UNOS status, and the mean score on the model for end-stage liver disease (MELD) system was 31 ± 8.9 (range, 11 - 40).

In group 2, 5 patients died during the first month following OLTx. The causes of death were intracerebral hemorrhage (n = 1), Candida glabrata infection (n = 1), bowel perforation (n = 1), and primary nonfunction (n = 2). Four patients required retransplantation, 2 for primary nonfunction, and 2 for hyperacute rejection. Complications included biliary stricture in 6 patients, primary nonfunction in 4 patients, hepatic artery thrombosis in 2 patients, hyperacute rejection in 1 patient, persistent coagulopathy in 1 patient, appendix perforation in 1 patient, and infection and sepsis in 2 patients.

Table 1. Etiology of underlying liver disease

Etiologies	Number of patients (n)	Percentage (%)
FHF	8	14.8
Autoimmune liver diseases	8	14.8
HCV	5	9.2
A1AT	4	7.4
ETOH	4	7.4
HCV + ETOH	3	5.5
Cryptogenic	3	5.5
PBC	4	7.4
HCV + HCC	2	3.7
Biliary atresia	3	5.5
Primary nonfunction	2	3.7
Hemochromatosis	1	1.8
Byler's disease	1	1.8
Others (HAT, hyperoxaluria, familial intrahepatic cholestasis)	6	11.1

A1AT: Alpha-1 antitrypsin deficiency
PBC: Primary biliary cirrhosis
PNF: Primary nonfunction
ETOH: Alcohol
HAT: Hepatic artery thrombosis
HCV: Hepatitis C virus
HCC: Hepatocellular cancer
FHF: Fulminant hepatic failure

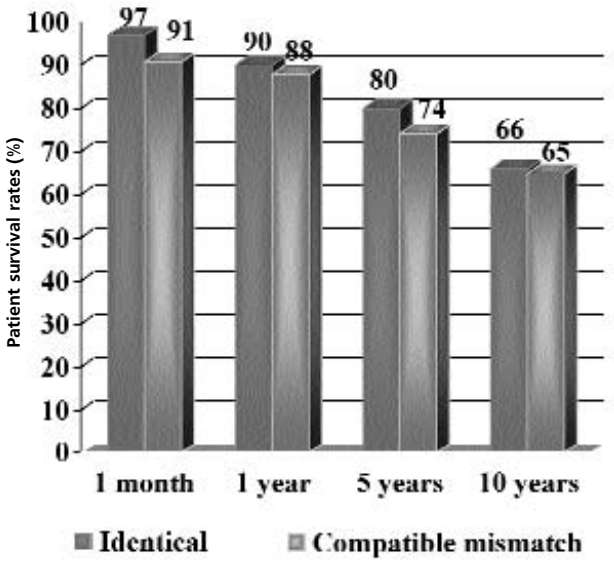

Figure 1. Kaplan-Meier *patient* survival rates for identical and compatible mismatched groups ($P > .05$)

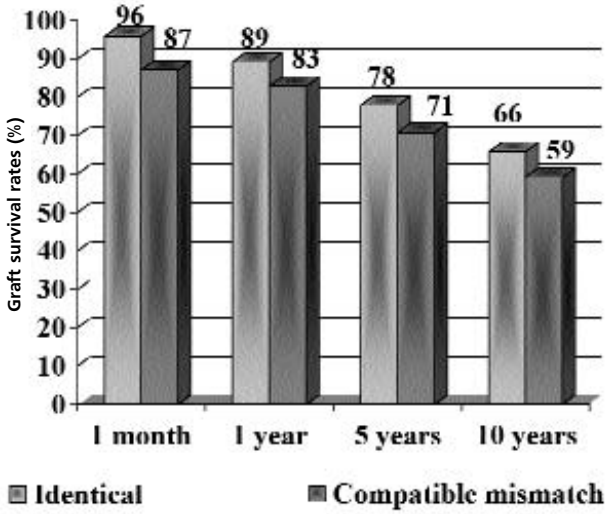

Figure 2. Kaplan-Meier *graft* survival rates for identical and compatible mismatch groups ($P > .05$)

Discussion

Use of ABO-incompatible grafts is considered to be contraindicated in OLTx to avoid hyperacute rejection. ABO-incompatible OLTx should be performed only under life-threatening situations, that is, for fulminant liver failure or primary nonfunction, which already carry very high mortality rates [4]. Ideally, soluble erythrocyte blood type antigens must be removed from circulation to protect the liver allograft, and plasmapheresis might be beneficial in this respect. Farges and coworkers found that plasmapheresis was highly effective in reducing anti-A/B antibody titers [4]. In our center, plasmapheresis is performed in all patients, including the 1 patient who received an incompatible mismatched graft, who subsequently developed hyperacute rejection following the second graft, and immediately required the third graft. The patient died despite use of a compatible mismatch for a third graft. This raises the possibility of major alterations in the body's immune system, which can be difficult to treat despite complete plasma exchange.

Tanaka and coworkers have emphasized that no significant difference exists regarding the incidence of acute rejection in pediatric patients receiving ABO-compatible and ABO-identical living-related liver transplantations. Interestingly, they also found that the survival rate for patients in the ABO-compatible group was significantly higher than it was for patients in the ABO-identical group [5]. In our study, we found no significant difference in survival rates between those receiving ABO-compatible and those receiving ABO-identical OLTx.

In conclusion, ABO-compatible mismatch OLTx is unavoidable in light of the current organ shortage. Our results suggest that this type of OLTx can be performed with minimal risk among patients with high UNOS/MELD statuses who require urgent transplantation.

References

1. Chui AK, Ling J, McCaughan GW, Painter D, Shun A, Dorney SF, et al. ABO blood group incompatibility in liver transplantation: A single-center experience. Aust N Z J Surg 1997; 67: 275-278
2. Gordon RD, Iwatsuki S, Esquivel CO, Tzakis A, Todo S, Starzl TE. Liver transplantation across ABO blood groups. Surgery 1986; 100: 342-348
3. Lang M, Neumann UP, Seinmuller T, Neuhaus P. Liver transplantation across ABO blood groups. Transplant Proc 2002; 34: 1501-1502
4. Farges O, Kalil AN, Samuel D, Saliba F, Arulnaden JL, Debat P, et al. The use of ABO-incompatible grafts in liver transplantation: a life-saving procedure in highly selected patients. Transplantation 1995; 59: 1124-1133
5. Tanaka A, Tanaka K, Kitai T, Yanabu N, Tokuka A, Sato B, et al. Living related liver transplantation across ABO blood groups. Transplantation 1994; 58: 548-553